

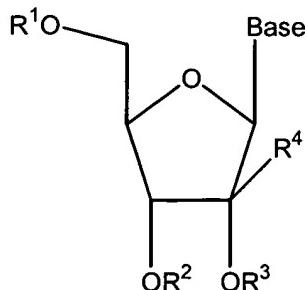
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- 1-32. (cancelled)
33. (currently amended): A method for treating a *Flaviviridae* infection in a host, comprising administering an effective amount of a 2'-branched nucleoside, or its pharmaceutically acceptable prodrug or salt to the host, optionally in a pharmaceutically acceptable carrier or diluent, in combination and/or alternation with one or more drugs that directly or indirectly induce a mutation in a *Flaviviridae* at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XR_XSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region, ~~and/or one or more drugs that are associated with such a mutation.~~
34. (currently amended): The method of claim 33 wherein the drug is a drug that directly or indirectly induces or is associated with a mutation in a *Flaviviridae* at a location other than nucleotide 1214 (G to C) or 405 Ser to Thr of the RNA polymerase region of BVDV or nucleotide 8443 (G to C) of the HCV genome or 282 Ser to Thr of the RNA polymerase region of HCV.
- 35-36. (cancelled)
37. (currently amended): The method ~~of any one of claims~~ claim 33 or 34-36, wherein the 2'-branched nucleoside is a 2'-branched pyrimidine nucleoside.
38. (previously presented): The method of claim 37, wherein the 2'-branched nucleoside is β-D-2'-CH₃-riboC.
39. (previously presented): The method of claim 37, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH₃-riboC.

40. (currently amended): The method of claim 39, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β -D-2'-CH₃-riboC.
41. (currently amended): The method of ~~any one of claims~~ claim 33 or 34 -36, wherein the 2'-branched nucleoside is a 2'-branched purine nucleoside.
42. (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is β -D-2'-CH₃-riboA.
43. (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β -D-2'-CH₃-riboA.
44. (previously presented): The method of claim 43, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β -D-2'-CH₃-riboA.
45. (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is β -D-2'-CH₃-ribo-6-N-methylaminopurine.
46. (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β -D-2'-CH₃-ribo-6-N-methylaminopurine.
47. (previously presented): The method of claim 46, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β -D-2'-CH₃-ribo-6-N-methylaminopurine.
48. (currently amended): The method of ~~any one of claims~~ claim 33 or 34 -36, wherein the 2'-branched nucleoside is of the formula:



or its pharmaceutically acceptable prodrug and/or salt, wherein R¹, R², and R³ are independently is H; ; mono, di or triphosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl

(including lower alkyl); sulfonate ester (including alkyl or arylalkyl sulfonyl including methanesulfonyl); benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; lipid (including a phospholipid); an amino acid ester; a carbohydrate; a peptide; cholesterol; or a pharmaceutically acceptable leaving group that provides a compound wherein R¹, R² or R³ is independently H or phosphate when administered *in vivo*; and

R² is acyl, an amino acid ester, a carbohydrate, a peptide or a pharmaceutically acceptable leaving group that provides a compound wherein R² is H or phosphate when administered *in vivo*;

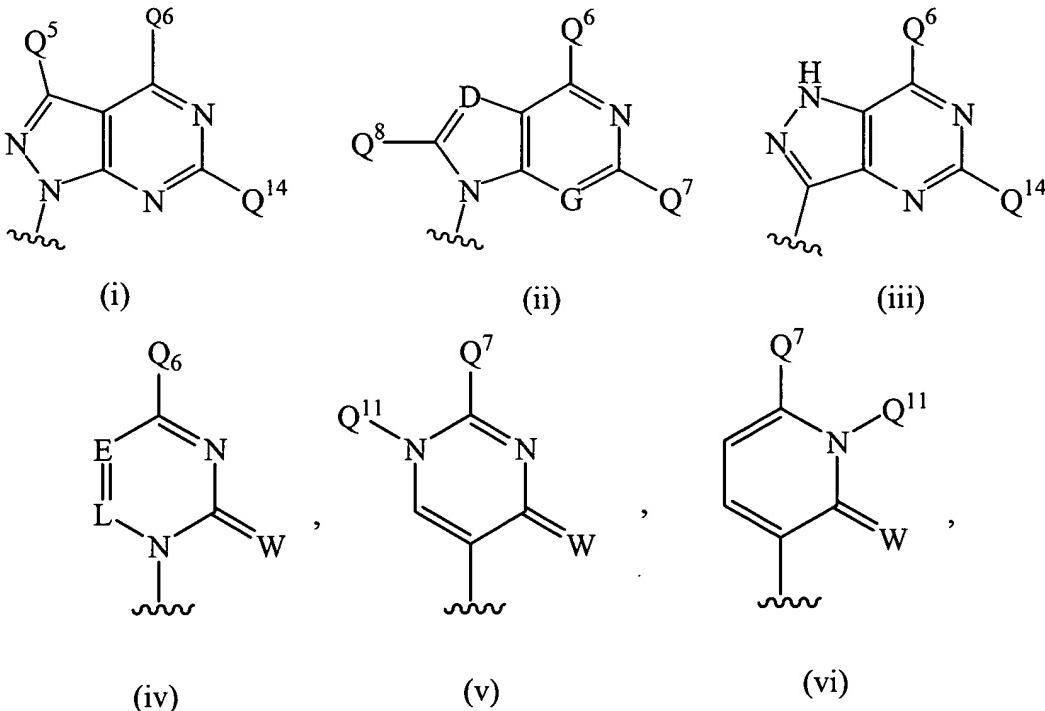
R³ is hydrogen;

R⁴ is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br vinyl, C(O)O(alkyl), C(O)O(lower alkyl), O(acyl), O(lower acyl), O(alkyl), -O(lower alkyl), O(alkenyl), chloro, bromo, fluoro, iodo, NO₂, NH₂, NH(lower alkyl), NH(acyl), N(lower alkyl)₂, or N(acyl)₂;

and Base is a purine or pyrimidine.

49. (currently amended): The method of claim 48, wherein base is selected from the group consisting of adenine, N⁶-alkylpurines, N⁶-acylpurines (wherein, wherein acyl is CO-alkyl, CO-aryl, CO-alkylaryl or CO-arylalkyl; C(O)(alkyl, aryl, alkylaryl, or arylalkyl), N⁶-benzylpurine, N⁶-halopurine, N⁶-vinylpurine, N⁶-acetylenic purine, N⁶-acyl purine, N⁶-hydroxyalkyl purine, N⁶-thioalkyl purine, N²-alkylpurines, N²-alkyl-6-thiopurines, thymine, cytosine, 5-fluorocytosine, 5-methylcytosine, 6-azapyrimidine, including 6-azacytosine, 2-mercaptopurine and/or 4-mercaptopurine 4-mercaptopurine, uracil, 5-halouracil, including 5-fluorouracil, C⁵-alkylpyrimidines, C⁵-benzylpyrimidines, C⁵-halopyrimidines, C⁵-vinyl-pyrimidine, C⁵-acetylenic pyrimidine, C⁵-acyl pyrimidine, C⁵-hydroxyalkyl purine, C⁵-amidopyrimidine, C⁵-cyanopyrimidine, C⁵-nitropyrimidine, C⁵-amino-pyrimidine, N²-alkylpurines, N²-alkyl-6-thiopurines, 5-azacytidinyl, 5-aza-uracilyl, triazolopyridinyl, imidazolopyridinyl, pyrrolopyrimidinyl, and pyrazolopyrimidinyl.

50. (currently amended): The method of claim 49, wherein base is of the formula:



wherein:

G and L are each independently CH or N;

D is N, CH, C-CN, C-NO₂, C-C₁₋₃ alkyl, C-NHCONH₂, C-CONQ¹¹Q¹¹, C-CSNQ^{II}Q^{II}, CCOOQ¹¹, C-C(=NH)NH₂, C-hydroxy, C-C₁₋₃alkoxy, C-amino, C-C₁₋₄alkyl-amino, C-di(C₁₋₄ alkyl)amino, C-halogen, C-(1,3-oxazol-2-yl), C-(1,3-thiazol-2-yl), or C-(imidazol-2-yl); wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C₁₋₃ alkoxy;

E is N or CQ⁵;

W is O, S, or NR;

R is H, OH, or alkyl;

Q⁶ is H, OH, SH, NH₂, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, C₃₋₆ cycloalkylamino, or halogen, C₁₋₄ alkyl, C₁₋₄ alkoxy, or CF₃;

Q⁵ is H, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₄ alkylamino, CF₃, halogen, N, CN, NO₂, NHCONH₂, CONQ¹¹Q¹¹, CSNQ^{II}Q^{II}, COOQ¹¹, C(=NH)NH₂, hydroxy, C₁₋₃alkoxy, amino, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, halogen, 1,3-oxazol-2-yl, 1,3-

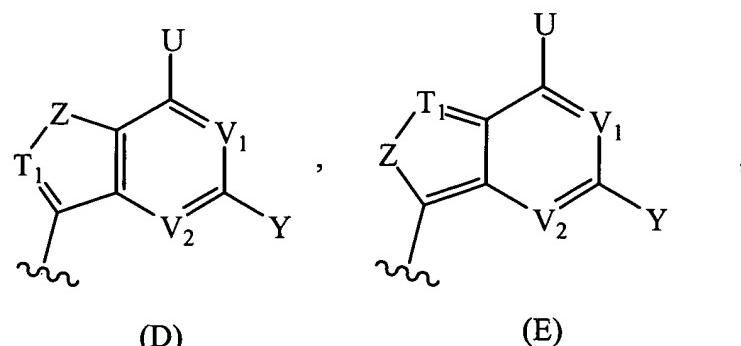
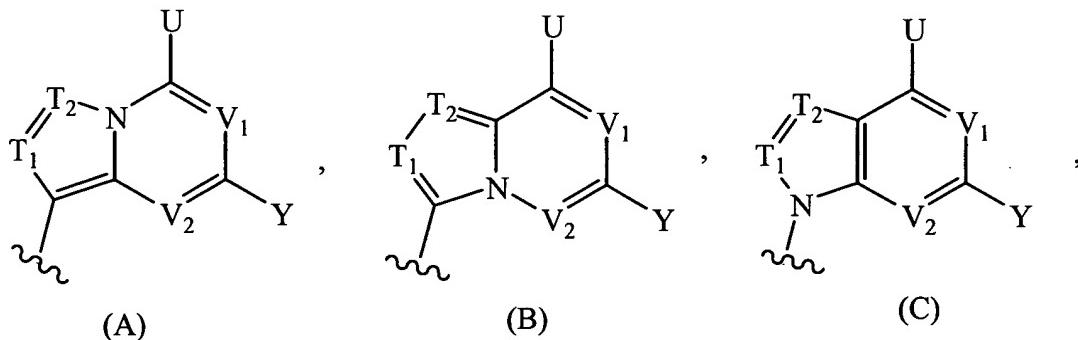
thiazol-2-yl, or imidazol-2-yl; wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C₁₋₃ alkoxy;

Q^7 and Q^{14} are each independently selected from the group consisting of H, CF₃, OH, SH, OR, SR C₁₋₄ alkyl, amino, C₁₋₄ alkylamino, C₃₋₆ cycloalkylamino, and di(C₁₋₄ alkyl)amino;

Q^{11} is independently H or C₁₋₆ alkyl; and

Q^8 is H, halogen, CN, carboxy, C_{1-4} alkyloxycarbonyl, N_3 , amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, hydroxy, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl) $_0$ - $_2$ aminomethyl, NH_2 , CN, NO_2 , C_{1-3} alkyl, $NHCONH_2$, $CONQ^{11}Q^{11}$, $CSNQ^{11}Q^{11}$, $COOQ^{11}$, $C(=NH)NH_2$, 1,3-oxazol-2-yl, 1,3-thiazol-2-yl, or imidazol-2-yl, wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C_{1-3} alkoxy.

51. (currently amended): The method of claim 49, wherein base is of the formula:



wherein:

T_1 and T_2 are independently selected from N, CH, or C-Q¹⁶;

Q^{16} , U, and Y are independently selected from is H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, cycloalkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4 OR^5 , NR^4R^5 NR^5R^6 or SR^5 , Br-vinyl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-aryl, -O-aralkyl, -O-acyl, -O-cycloalkyl, NH_2 , NH-alkyl, N-dialkyl, NH-acyl, N-aryl NH-aryl, N-aralkyl NH-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, CN, N_3 , COOH, CONH_2 , CO_2 -alkyl, CONH-alkyl, CON-dialkyl, OH, CF_3 , CH_2OH , $(\text{CH}_2)_m\text{OH}$, $(\text{CH}_2)_m\text{NH}_2$, $(\text{CH}_2)_m\text{COOH}$, $(\text{CH}_2)_m\text{CN}$, $(\text{CH}_2)_m\text{NO}_2$, $(\text{CH}_2)_m\text{CONH}_2$, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl)₂aminomethyl, or - $\text{NHC}(=\text{NH})\text{NH}_2$;

R^4 R^6 and R^5 are independently selected from hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl);

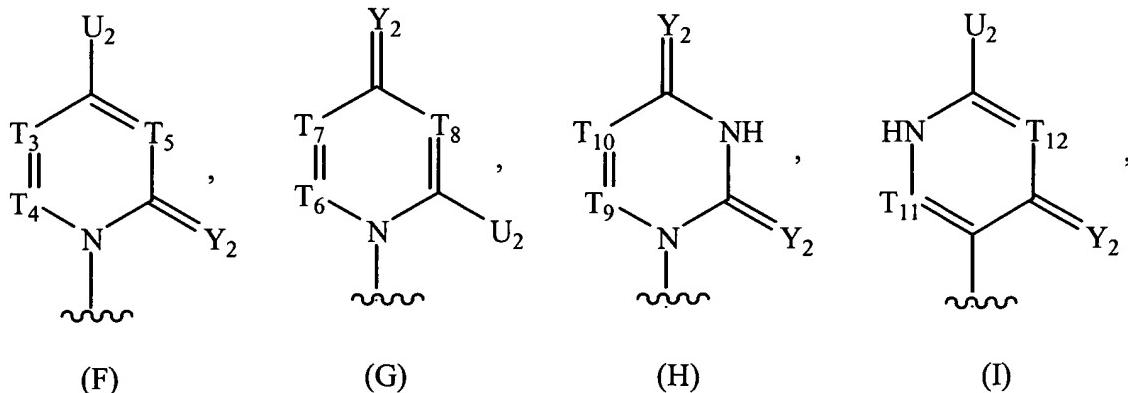
m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

Z is S, SO, SO_2 , C=O, or NQ^{20} ;

Q^{20} is H or alkyl; and

V_1 and V_2 are independently selected from CH or N.

52. (currently amended): The method of claim 49, wherein base is of the formula:



wherein:

T_3 and T_4 are independently selected from N or CQ^{22} ;

Q^{22} is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, cycloalkyl, CO-alkyl,

CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, $\text{OR}^4 \text{OR}^5$, $\text{NR}^4 \text{R}^5 \text{NR}^5 \text{R}^6$ or SR^5 , Br-vinyl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-aryl, -O-aralkyl, -O-acyl, -O-cycloalkyl, NH₂, NH-alkyl, N-dialkyl, NH-acyl, ~~N-aryl NH-aryl, N-aralkyl NH-aralkyl~~, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, CN, N₃, COOH, CONH₂, CO₂-alkyl, CONH-alkyl, CON-dialkyl, OH, CF₃, CH₂OH, (CH₂)_mOH, (CH₂)_mNH₂, (CH₂)_mCOOH, (CH₂)_mCN, (CH₂)_mNO₂, (CH₂)_mCONH₂, C₁₋₄ alkylamino, di(C₁₋₄ alkyl)amino, C₃₋₆ cycloalkylamino, C₁₋₄ alkoxy, C₁₋₄ alcoxycarbonyl, C₁₋₆ alkylthio, C₁₋₆ alkylsulfonyl, (C₁₋₄ alkyl)₀₋₂aminomethyl, or -NHC(=NH)NH₂;

T₅ is NH N;

R⁴ R⁶ and R⁵ are independently selected from hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl);

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

T₆, T₇, T₈, T₉, T₁₀, T₁₁, and T₁₂ are independently selected from N or CH;

U₂ is H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, $\text{OR}^4 \text{OR}^5$, $\text{NR}^4 \text{R}^5 \text{NR}^5 \text{R}^6$ or SR⁵;

Y₂ is O, S, NH, NR or CQ²⁴Q²⁶ where R is H, OH, or alkyl; and

Q²⁴ and Q²⁶ are independently selected from H, alkyl, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, $\text{OR}^4 \text{OR}^5$, $\text{NR}^4 \text{R}^5 \text{NR}^5 \text{R}^6$ or SR⁵.

53-86. (cancelled)

87. (new): The method of claim 48, wherein R¹ is a mono, di or triphosphate.

88. (new): The method of claim 48, wherein R² is acyl.

89. (new): The method of claim 48, wherein R² is an amino acid ester.

90. (new): The method of claim 48, wherein R² is a peptide or a carbohydrate.

91. (new): The method of claim 48, wherein R⁴ is alkyl.
92. (new): The method of claim 48, wherein R⁴ is methyl.
93. (new): The method of claim 48, wherein R⁴ is alkenyl or akynyl.
94. (new) The method of claim 93, wherein R⁴ is -CH=CH₂.
95. (new) The method of claim 95, wherein R⁴ is ethynyl.
96. (new) The method of claim 88, wherein acyl is of the formula C(O)R', wherein R' is a straight, branched, or cyclic alkyl.
97. (new) The method of claim 88, wherein acyl is of the formula C(O)R', wherein R' is aryl, alkaryl, aralkyl, alkoxyalkyl or aryloxyalkyl.
98. (new) The method of claim 88, wherein R² is acetyl.
99. (new) The method of claim 88, wherein R² is propionyl, butyryl, hexanoyl, or 2-propenyl.
100. (new) The method of claim 48, wherein R² is an ester of an amino acid selected from the group consisting of glycine, alanine, valine, leucine, isoleucine, methionine, phenylalanine, tryptophan, proline, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartate, glutamate, lysine, arginine and histidine.
101. (new) The method of claim 48, wherein R² is an ester of a naturally occurring or synthetic α, β, γ, or δ amino acid.
102. (new) The method of claim 48, wherein R² is an ester of an amino acid in the L configuration.

103. (new) The method of claim 48, wherein R² is an ester of valine.
104. (new) The method of claim 48, wherein:
R⁴ is methyl;
R² is acyl or an amino acid ester;
R³ is H; and
R¹ is H.
105. (new) The method of claim 104, wherein R² is an amino acid ester.
106. (new) The method of claim 104, wherein R² is an ester of valine.
107. (new) The method of any one of claim 33, 34, 48, or 104 wherein host is human.
108. (new) The method of any one of claim 33, 34 48, or 104 wherein the virus is hepatitis C.